Exhibit 1

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PHASE I TRIAL OF A 3 HOUR TAXOL INFUSION PLUS OR MINUS GRANULOCYTE-COLONY STIMULATING FACTOR (G-CSF). L.H. Schiller, K. Tutsch, R. Arzoomanian, D. Alberti, C. Feierabend, D. Spriggs. Univ. Wisconsin Comp. Cancer Center, Madison, WI 53792.

We are conducting a Phase I study to determine the Phase II dose and pharmacology of taxol administered over 3 hours with and without G-CSF. To date we have treated 20 patients (pts) with incurable malignancies with one of 3 dose levels of taxol every 3 weeks, ± G-CSF subcutaneously days 2-14. Endpoints include absolute neutrophil counts (ANC) < 500 (x 10^3/mm^3) for > 5 days, failure to recover counts on time for cycle 2, and other Grade (Gr) 3-4 toxicities. Mean nadir ANC (# pts) for course 1 are:

	Taxol (mg/m^2)		
	210	250	300
G-CSF (μg/kg/day)			
0	0.82 (4)*	0.84 (6)**	-- (0)
5	3.80 (4)	6.20 (3)	4.0 (3)

* 1 pt-ANC < 500 x 5 days; ** 2 pts-ANC < 500 x 6 days.

No clinically significant thrombocytopenia or arrhythmias have been observed. 2 pts at the lowest dose level developed Gr 2 peripheral neuropathies with repeated treatments; 1 pt at 300 mg/m^2 developed Gr 3 neurotoxicity; 15 pts have developed Gr 1 or 2 arthralgias. 2 pts have died (1-multiple arterial and venous thrombi; 1-sepsis unrelated to neutropenia). 2 pts have had partial responses (breast, ovary). Plasma taxol concentrations (C_p) were measured by HPLC in 16 pts. Mean (SD) peak C_p were 7.0(2.4), 9.9(1.7) and 12.5(2.7) μM at 210, 250 and 300 mg/m^2, respectively. Mean total body clearance was 7.9(1.4) L/h/m^2, mean V_c was 5.0(1.5) L/m^2 and mean terminal $t_{1/2}$ was 9.7 h. We conclude that 210 mg/m^2 of taxol as a 3 hour infusion is tolerable without G-CSF, and at least 250 mg/m^2 can be administered without dose limiting toxicity with G-CSF. Additional pts are being entered to further define the maximally tolerated dose with G-CSF. Support: NIH NO1-CM-07306; RR03186.

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SERUM DRUG LEVELS FOLLOWING CONTINUOUS INFUSION ETOPOSIDE. J. Levin, G. Parkhurst and P. Bonomi. Rush Medical College, Chicago, IL. 60612

It has been postulated that prolonged administration of low dose etoposide is more effective and less toxic than repeat bolus dosing in patients with small cell lung cancer and that maintenance of serum drug levels above 1 ug/ml might produce optimal results. This study was performed to determine what dosage of intravenous etoposide yields the desired serum levels, what toxicity results, and what factors affect serum levels. Seventeen patients with locally advanced or metastatic cancer were treated with continuous infusion intravenous etoposide at doses of 30, 40 or 50 mg/m^2/24 hr. Treatment lasted for 4,5 or 10 days. The majority of patients also received concurrent radiation therapy and cisplatinum (60 mg/m^2 on day 1). Serum samples for drug levels were obtained 36 to 60 hours after treatment began in order to assure achievement of steady-state levels. Serum etoposide concentrations were determined by HPLC with a reverse-phase C_{18} column using electrochemical detection. Infusions of 30, 40 and 50 mg/m^2/24 hr. resulted in serum concentrations of 1.02 ± 0.025 (N=6), 1.30 ± 0.51 (N=8) and 1.81 ± 0.44 ug/ml(N=4) respectively. Significant myelosuppression (nadir WBC=2.5) was observed in only one patient who received 50 mg/m^2 for 5 days. No severe adverse reactions occurred. In these patients, serum drug levels did not appear to be affected by serum creatinine, albumin, bilirubin or concurrent cisplatinum administration. The results show that serum etoposide levels in the target range can be obtained with continuous low dose infusion of drug in the range of 30-40 mg/m^2/24 hr. in patients with normal renal and hepatic function. It is likely that these levels can be maintained for longer periods of time than done here without causing major toxicity. Further studies are planned to determine the efficacy and toxicity of more prolonged dosing schedules.

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PROGRAM/PROCEEDINGS

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